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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/835,119	04/13/2001	Rima Kaddurah-Daouk	MBZ-001	4219

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Elizabeth A. Hanley, Esq.
Lahive & Cockfield, LLP
28 State Street
Boston, MA 02109

EXAMINER	
CHAKRABARTI, ARUN K	
ART UNIT	PAPER NUMBER
1634	7

DATE MAILED: 05/16/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Office Action Summary	Application No.	Applicant(s)	
	09/835,119	KADDURAH-DAOUK ET AL.	
	Examiner	Art Unit	
	Arun Chakrabarti	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 April 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-55* is/are pending in the application.

4a) Of the above claim(s) *1-3 and 5-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4 and 20-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*.

DETAILED ACTION

Specification

1. Applicant's election of Group III, corresponding to claims 4, and 20-55, without traverse, in Paper NO: 6, is hereby acknowledged.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 4, and 20-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 and 20-55 are vague and indefinite over the recitation of the phrase, "small molecules". The term "small molecules" in claims 4, 20, 26, 27, 36, 37, 44, 48, 49, 54, and 55 is a relative term which renders the claims indefinite. The term "small molecules" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claims 21, 33, and 38 are rejected over the recitation of the phrase, "cellular compartment is a cell (s)". It is not clear if a compartment of the cell is claimed or the whole cell is claimed or both is claimed. The metes and bounds of the claims are vague.

Claims 30 and 32 are rejected over the recitation of the phrase, "other disorder". In absence of a definition of "other" in the specification and the claim, the metes and bounds of the claims are vague and indefinite because it is not clear what disorders are claimed in the invention.

Regarding claim 48, the phrase "searchable" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention.

Claim 55 is vague and indefinite as it is dependent on a non-elected claim 1. Appropriate correction is suggested.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 20-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 20-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of identifying human tumor does not reasonably provide enablement for identifying any disease in any living organism. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The Court in re Wands, 8 USPQ2d 1400 (CA FC 1988) stated with regard to enablement that

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

Here, the claim is broadly drawn to identifying any disease in any living species. However, the specification does not provide guidance commensurate in scope with this claim, teaching only one human tumor detection assay in Example 6. The specification provides minimal guidance regarding methods for the identification of alternate diseases. It is highly unpredictable whether or what other diseases would be detected in the context of a vast database of diseases. Further, identification of additional disease detection regiment will be by the trial and error method. This trial and error requirement is borne out because the effects of diseases on metabolites or small molecules of the physiological system cannot be readily deduced, even where the metabolic pathways are known. Further, each disease has unpredictable effects on metabolic function, and no general method for a priori selection of disease detection is presented. It would require a large amount of experimentation, potentially including the testing of thousands of animals for thousands of diseases, in order to identify additional metabolic pathways with the

claimed functionality. Given the Wand's factors opposing the full scope of enablement including the limited teaching in the specification, the presence of only one working example, the teaching of unpredictability in the prior art, the unpredictability of the art, the breadth of the claim, and the large amount of experimentation needed, with only the skill level in the art being neutral towards enablement, it is concluded that undue experimentation is necessary to make and use the invention as broadly claimed.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

7. Claims 4, 20-21, 23-33, 35-38, 40-50, 52, and 55 are rejected under 35 U.S.C. 102(e) as being anticipated by Kaser et al. (U.S. Patent 6,168,933 B1) (January 2, 2001).

Kaser et al teach a method for metabolomically monitoring the effectiveness of a therapeutic agent in a clinical trial (Abstract and Column 1, lines 22-25), comprising:

a) obtaining a small molecule profile from a subject in a clinical trial being treated with a

therapeutic agent (Column 15, line 45 to Column 16, line 24 and Column 11, lines 40-44, and Column 13, lines 1-10); and

b) monitoring changes in the small molecule profile of the subject as an indication of the effectiveness of the therapeutic agent in the subject, thereby monitoring the effectiveness of the therapeutic agent (Column 15, line 45 to Column 16, line 24).

Kaser et al teach a method for identifying disease relevant small molecules affected by an agent (Abstract) comprising:

a) obtaining a small molecule profile of a diseased cellular compartment (Column 11, line 40 to Column 12, line 51); and

b) comparing the small molecule profile of the diseased cell to a standard small molecule profile (Column 12, lines 52-67), thereby identifying the disease relevant small molecules in the diseased cellular compartment (Column 13, lines 12-22 and Column 26, lines 10-25).

Kaser et al teach a method for identifying small molecules regulated, modulated, or associated with a gene (abstract), comprising:

a) obtaining a small molecule profile of a cellular compartment from a genetically modified source (Column 14, lines 48-60); and

b) comparing the small molecule profile to a standard small molecule profile, thus identifying the small molecules regulated, modulated, or associated with a gene (Column 12, lines 52-67).

Kaser et al teach a method for identifying potential cell drug targets (Column 15, lines 45-

58), comprising:

a) contacting a labeled disease relevant small molecule with cellular components in a nucleic acid or protein array (Column 16, lines 1-17); and

b) identifying interactions between the cell components and the labeled disease relevant small molecule, thus identifying potential cell drug targets (Column 16, lines 17-24).

Kaser et al teach a library of small molecules of a cellular compartment of a cell comprising a searchable array of samples of small molecules isolated from a cellular compartment of an animal cell nucleus (Column 15, line 45 to Column 16, line 24 and Column 3, lines 2-6).

Kaser et al teach a pharmaceutical composition comprising a small molecule which enables to detect a diseased state (Column 16, lines 25-49).

Kaser et al teach the methods, wherein the diseased cellular compartments are human cells and nuclei obtained from patients with metabolic, immunological, neurological, oncological, viral, or other disorder (Column 13, line 36 to Column 14, line 31)

Kaser et al teach a method wherein the small molecule profiles are obtained using radiochemical analysis and fluorescent analysis (Column 13, lines 12-22).

Kaser et al teach a method wherein the expression vector is a portion of the human genome (Column 8, line 54 to column 9, line 60 and Column 19, line 20 to Column 20, line 9).

8. Claims 20, 22, 48, 51, and 54 are rejected under 35 U.S.C. 102(e) as being anticipated by

Polyak et al. (U.S. Patent 6,344,322 B1) (February 5, 2002).

Polyak et al. teach a method for identifying disease relevant small molecules affected by an agent (Abstract) comprising:

a) obtaining a small molecule profile of a diseased cellular compartment (Example 1); and

b) comparing the small molecule profile of the diseased cell to a standard small molecule profile thereby identifying the disease relevant small molecules in the diseased cellular mitochondrial compartment (Example 1 and Figure 1).

Polyak et al teach a library of small molecules of a cellular compartment of a cell comprising a searchable array of samples of small molecules isolated from a cellular compartment of an animal cell mitochondria (Figure 1).

Polyak et al inherently teach a method for determining whether small molecule profiles are from the same individual, comprising:

a) obtaining one or more samples from an individual;

b) determining the small molecule profiles of the samples;

c) obtaining a tissue sample from an unknown source;

d) determining the small molecule profiles of the unknown source; and

e) comparing the small molecule profiles, thus determining whether the small molecule profiles are from the same individual (Column 3, line 56 to Column 4, line 59).

9. Claims 48, and 53 are rejected under 35 U.S.C. 102(e) as being anticipated by

Ward et al. (U.S. Patent 5,541,310) (July 30, 1996).

Ward et al teach a library of small molecules of a cellular compartment of a cell comprising a searchable array of samples of small molecules isolated from a cellular compartment of a chloroplast (Abstract and Examples 1-4).

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 4, 20-21, 23-50, 52, and 55 are rejected under 35 U.S.C. 103(a) over Kaser et al. (U.S. Patent 6,168,933 B1) (January 2, 2001) in view of Polyak et al. (U.S. Patent 6,344,322 B1) (February 5, 2002)..

Kaser et al teach the method of claims 4, 20-21, 23-33, 35-38, 40-50, 52, and 55 as described above.

Kaser et al do not teach the method wherein the cellular compartment is mitochondria.

Polyak et al. teach the method wherein the cellular compartment is mitochondria (Abstract, Example 1 and Figure 1).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the method wherein the cellular compartment is mitochondria of Polyak et al in the method of Kaser et al., since Polyak et al. states, "The invention thus provides the art with new methods of detecting and tracing tumors by examining mitochondrial DNA for the appearance of somatic mutations (Column 1, lines 44-46)." An ordinary practitioner would have been motivated to substitute and combine the method wherein the cellular compartment is mitochondria of Polyak et al in the method of Kaser et al in order to achieve the express advantages, as noted by Polyak et al. of an invention which provides the art with new methods of detecting and tracing tumors by examining mitochondrial DNA for the appearance of somatic mutations.

Conclusion

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this

Group is (703) 305-7401. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

Arun Chakrabarti,

Patent Examiner,

May 2, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600